

Porphyria

National Digestive Diseases Information Clearinghouse



What are porphyrias?

Porphyrias are rare disorders that affect mainly the skin or nervous system and may cause abdominal pain. These disorders are usually inherited, meaning they are caused by abnormalities in genes passed from parents to children. When a person has a porphyria, cells fail to change body chemicals called porphyrins and porphyrin precursors into heme, the substance that gives blood its red color. The body makes heme mainly in the bone marrow and liver. Bone marrow is the soft, spongelike tissue inside the bones; it makes stem cells that develop into one of the three types of blood cells—red blood cells, white blood cells, and platelets.

The process of making heme is called the heme biosynthetic pathway. One of eight enzymes controls each step of the process. The body has a problem making heme if any one of the enzymes is at a low level, also called a deficiency. Porphyrins and porphyrin precursors of heme then build up in the body and cause illness.

What is heme and what does it do?

Heme is a red pigment composed of iron linked to a chemical called protoporphyrin. Heme has important functions in the body. The largest amounts of heme are in the form of hemoglobin, found in red blood cells and bone marrow. Hemoglobin carries oxygen from the lungs to all parts of the body. In the liver, heme is a component of proteins that break down hormones, medications, and other chemicals and keep liver cells functioning normally. Heme is an important part of nearly every cell in the body.

What are the types of porphyria?

Each of the eight types of porphyria corresponds to low levels of a specific enzyme in the heme biosynthetic pathway. Experts often classify porphyrias as acute or cutaneous based on the symptoms a person experiences:

- Acute porphyrias affect the nervous system. They occur rapidly and last only a short time.
- Cutaneous porphyrias affect the skin.

Two types of acute porphyrias, hereditary coproporphyria and variegate porphyria, can also have cutaneous symptoms.

Experts also classify porphyrias as erythropoietic or hepatic:

- In erythropoietic porphyrias, the body overproduces porphyrins, mainly in the bone marrow.
- In hepatic porphyrias, the body overproduces porphyrins and porphyrin precursors, mainly in the liver.

Table 1 lists each type of porphyria, the deficient enzyme responsible for the disorder, and the main location of porphyrin buildup.

How common is porphyria?

The exact rates of porphyria are unknown and vary around the world. For example, porphyria cutanea tarda is most common in the United States, and variegate porphyria is most common in South America.¹

What causes porphyria?

Most porphyrias are inherited disorders. Scientists have identified genes for all eight enzymes in the heme biosynthetic pathway. Most porphyrias result from inheriting an abnormal gene, also called a gene mutation, from one parent. Some porphyrias, such as congenital erythropoietic porphyria,

Table 1. Types of porphyria

Type of Porphyria	Deficient Enzyme	Main Location of Porphyrin Buildup
delta-aminolevulinate-dehydratase deficiency porphyria	delta-aminolevulinic acid dehydratase	liver
acute intermittent porphyria	porphobilinogen deaminase	liver
hereditary coproporphyria	coproporphyrinogen oxidase	liver
variegate porphyria	protoporphyrinogen oxidase	liver
congenital erythropoietic porphyria	uroporphyrinogen III cosynthase	bone marrow
porphyria cutanea tarda	uroporphyrinogen decarboxylase (~75% deficiency)	liver
hepatoerythropoietic porphyria	uroporphyrinogen decarboxylase (~90% deficiency)	bone marrow
erythropoietic protoporphyria*	ferrochelatase (~75% deficiency)	bone marrow

*Protoporphyria XLPP is a variant of erythropoietic protoporphyria.

¹Pierach CA. Porphyrias. In: Bope and Kellerman, eds. *Conn's Current Therapy 2012*. 1st ed. Philadelphia, PA: Saunders; 2011: 847–850.

hepatoerythropoietic porphyria, and erythropoietic protoporphyria, occur when a person inherits two abnormal genes, one from each parent. The likeliness of a person passing the abnormal gene or genes to the next generation depends on the type of porphyria.

Porphyria cutanea tarda is usually an acquired disorder, meaning factors other than genes cause the enzyme deficiency. This type of porphyria can be triggered by

- too much iron
- use of alcohol or estrogen
- smoking
- chronic hepatitis C—a long-lasting liver disease that causes inflammation, or swelling, of the liver
- HIV—the virus that causes AIDS
- abnormal genes associated with hemochromatosis—the most common form of iron overload disease, which causes the body to absorb too much iron

For all types of porphyria, symptoms can be triggered by

- use of alcohol
- smoking
- use of certain medications or hormones
- exposure to sunlight
- stress
- dieting and fasting

What are the symptoms of porphyria?

Some people with porphyria-causing gene mutations have latent porphyria, meaning they have no symptoms of the disorder. Symptoms of cutaneous porphyrias include

- oversensitivity to sunlight
- blisters on exposed areas of the skin
- itching and swelling on exposed areas of the skin

Symptoms of acute porphyrias include

- pain in the abdomen—the area between the chest and hips
- pain in the chest, limbs, or back
- nausea and vomiting
- constipation—a condition in which an adult has fewer than three bowel movements a week or a child has fewer than two bowel movements a week, depending on the person
- urinary retention—the inability to empty the bladder completely
- confusion
- hallucinations
- seizures and muscle weakness

Symptoms of acute porphyrias can develop over hours or days and last for days or weeks. These symptoms can come and go over time, while symptoms of cutaneous porphyrias tend to be more continuous. Porphyria symptoms can vary widely in severity.

How is porphyria diagnosed?

A health care provider diagnoses porphyria with blood, urine, and stool tests. These tests take place at a health care provider's office or a commercial facility. A blood test involves drawing blood and sending the sample to a lab for analysis. For urine and stool tests, the patient collects a sample of urine or stool in a special container. A health care provider tests the samples in the office or sends them to a lab for analysis. High levels of porphyrins or porphyrin precursors in blood, urine, or stool indicate porphyria. A health care provider may also recommend DNA testing of a blood sample to look for known gene mutations that cause porphyrias.

How is porphyria treated?

Treatment for porphyria depends on the type of porphyria the person has and the severity of the symptoms.

Acute Porphyrias

A health care provider treats acute porphyrias with heme or glucose loading to decrease the liver's production of porphyrins and porphyrin precursors. A patient receives heme intravenously once a day for 4 days. Glucose loading involves giving a patient a glucose solution by mouth or intravenously. Heme is usually more effective and is the treatment of choice unless symptoms are mild. In

rare instances, if symptoms are severe, a health care provider will recommend liver transplantation to treat acute porphyria. In liver transplantation, a surgeon removes a diseased or an injured liver and replaces it with a healthy, whole liver or a segment of a liver from another person, called a donor. A patient has liver transplantation surgery in a hospital under general anesthesia. Liver transplantation can cure liver failure. Read more in *Liver Transplantation* at www.digestive.niddk.nih.gov.

Cutaneous Porphyrias

The most important step a person can take to treat a cutaneous porphyria is to avoid sunlight as much as possible. Other cutaneous porphyrias are treated as follows:

- **Porphyria cutanea tarda.** A health care provider treats porphyria cutanea tarda by removing factors that tend to activate the disease and by performing repeated therapeutic phlebotomies to reduce iron in the liver. Therapeutic phlebotomy is the removal of about a pint of blood from a vein in the arm. A technician performs the procedure at a blood donation center, such as a hospital, clinic, or bloodmobile. A patient does not require anesthesia. Another treatment approach is low-dose hydroxychloroquine tablets to reduce porphyrins in the liver.

- **Erythropoietic protoporphyria.** People with erythropoietic protoporphyria may be given beta-carotene or cysteine to improve sunlight tolerance, though these medications do not lower porphyrin levels. Experts recommend hepatitis A and B vaccines and avoiding alcohol to prevent protoporphyric liver failure. A health care provider may use liver transplantation or a combination of medications to treat people who develop liver failure. Unfortunately, liver transplantation does not correct the primary defect, which is the continuous overproduction of protoporphyria by bone marrow. Successful bone marrow transplantations may successfully cure erythropoietic protoporphyria. A health care provider only considers bone marrow transplantation if the disease is severe and leading to secondary liver disease.
- **Congenital erythropoietic porphyria and hepatoerythropoietic porphyria.** People with congenital erythropoietic porphyria or hepatoerythropoietic porphyria may need surgery to remove the spleen or blood transfusions to treat anemia. A surgeon removes the spleen in a hospital, and a patient receives general anesthesia. With a blood transfusion, a patient receives blood through an intravenous (IV) line inserted into a vein. A technician performs the procedure at a blood donation center, and a patient does not need anesthesia.

Secondary Porphyrinurias

Conditions called secondary porphyrinurias, such as disorders of the liver and bone marrow, as well as a number of drugs, chemicals, and toxins are often mistaken for porphyria because they lead to mild or moderate increases in porphyrin levels in the urine. Only high—not mild or moderate—levels of porphyrin or porphyrin precursors lead to a diagnosis of porphyria.

Eating, Diet, and Nutrition

People with an acute porphyria should eat a diet with an average-to-high level of carbohydrates. The recommended dietary allowance for carbohydrates is 130 g per day for adults and children 1 year of age or older; pregnant and breastfeeding women need higher intakes.² People should avoid limiting intake of carbohydrates and calories, even for short periods of time, as this type of dieting or fasting can trigger symptoms. People with an acute porphyria who want to lose weight should talk with their health care providers about diets they can follow to lose weight gradually.

People undergoing therapeutic phlebotomies should drink plenty of milk, water, or juice before and after each procedure.

A health care provider may recommend vitamin and mineral supplements for people with a cutaneous porphyria.

²National Research Council. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*. Washington, D.C.: The National Academies Press; 2005.

Points to Remember

- Porphyrias are rare disorders that affect mainly the skin or nervous system and may cause abdominal pain.
- Each of the eight types of porphyria corresponds to low levels of a specific enzyme in the heme biosynthetic pathway.
- The exact rates of porphyria are unknown and vary around the world. For example, porphyria cutanea tarda is most common in the United States, and variegate porphyria is most common in South America.
- Most porphyrias result from inheriting an abnormal gene, also called a gene mutation, from one parent.
- Porphyria cutanea tarda is usually an acquired disorder, meaning factors other than genes cause the enzyme deficiency.
- Symptoms of cutaneous porphyrias include
 - oversensitivity to sunlight
 - blisters on exposed areas of the skin
 - itching and swelling on exposed areas of the skin
- Symptoms of acute porphyrias include
 - pain in the abdomen
 - pain in the chest, limbs, or back
 - nausea and vomiting
 - constipation
 - urinary retention
 - confusion
 - hallucinations
 - seizures and muscle weakness
- A health care provider diagnoses porphyria with blood, urine, and stool tests.
- Treatment for porphyria depends on the type of porphyria the person has and the severity of the symptoms.

Hope through Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports research to help people with digestive diseases, including disorders that affect the liver.

Clinical trials are research studies involving people. Clinical trials look at safe and effective new ways to prevent, detect, or

treat disease. Researchers also use clinical trials to look at other aspects of care, such as improving the quality of life for people with chronic illnesses. To learn more about clinical trials, why they matter, and how to participate, visit the NIH Clinical Research Trials and You website at www.nih.gov/health/clinicaltrials. For information about current studies, visit www.ClinicalTrials.gov.

For More Information

For more information about porphyria, see the following online publications:

Learning about Porphyria, available from the National Human Genome Research Institute at www.genome.gov/19016728.

Porphyria, available from the U.S. National Library of Medicine's Genetics Home Reference at www.ghr.nlm.nih.gov/condition=porphyria.

Information about porphyria is also available from the following organizations:

American Porphyria Foundation

4900 Woodway, Suite 780
Houston, TX 77056-1837
Phone: 1-866-APF-3635 (1-866-273-3635)
or 713-266-9617
Fax: 713-840-9552
Email: porphyrus@aol.com
Internet: www.porphyriafoundation.com

Iron Disorders Institute

P.O. Box 675
Taylors, SC 29687
Phone: 1-888-565-IRON (1-888-565-4766)
or 864-292-1175
Email: cgarrison@irondisorders.org
Internet: www.irondisorders.org

National Institutes of Health Office of Rare Diseases Research Genetic and Rare Diseases Information Center

P.O. Box 8126
Gaithersburg, MD 20898-8126
Phone: 1-888-205-2311 or 301-251-4925
TTY: 1-888-205-3223
Internet: www.rarediseases.info.nih.gov/GARD

National Organization for Rare Disorders

55 Kenosia Avenue
Danbury, CT 06810
Phone: 1-800-999-6673 or 203-744-0100
Fax: 203-798-2291
Internet: www.rarediseases.org

The Porphyrins Consortium

Dana O. Doheny, M.S., C.G.
Consortium Project Coordinator
Mount Sinai School of Medicine
Department of Genetics and Genomic Sciences
1425 Madison Avenue, 14-75A
New York, NY 10029
Phone: 1-866-322-7968 or 212-659-6779
Fax: 212-659-6780
Email: dana.doheny@mssm.edu
Internet: <http://rarediseasesnetwork.epi.usf.edu/porphyrias>

Acknowledgments

Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This publication was reviewed by Herbert L. Bonkovsky, M.D., Carolinas Health Care System, Charlotte, NC.

You may also find additional information about this topic by visiting MedlinePlus at www.medlineplus.gov.

This publication may contain information about medications and, when taken as prescribed, the conditions they treat. When prepared, this publication included the most current information available. For updates or for questions about any medications, contact the U.S. Food and Drug Administration toll-free at 1-888-INFO-FDA (1-888-463-6332) or visit www.fda.gov. Consult your health care provider for more information.

National Digestive Diseases Information Clearinghouse

2 Information Way
Bethesda, MD 20892-3570
Phone: 1-800-891-5389
TTY: 1-866-569-1162
Fax: 703-738-4929
Email: nddic@info.niddk.nih.gov
Internet: www.digestive.niddk.nih.gov

The National Digestive Diseases Information Clearinghouse (NDDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health of the U.S. Department of Health and Human Services. Established in 1980, the Clearinghouse provides information about digestive diseases to people with digestive disorders and to their families, health care professionals, and the public. The NDDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about digestive diseases.

This publication is not copyrighted. The Clearinghouse encourages users of this publication to duplicate and distribute as many copies as desired.

This publication is available at
www.digestive.niddk.nih.gov.



National Institute of
Diabetes and Digestive
and Kidney Diseases

NIH Publication No. 14-4632
December 2013